

AMENDMENTS TO THE CLAIMS

Please cancel claims 1-39 without prejudice.

40. (New) A nucleic acid molecule encoding a heregulin variant having an amino acid sequence not found in nature and the ability to bind an ErbB receptor, wherein
- said variant comprises a methionine residue in place of amino acid residues corresponding to residue numbers 228 to 231 of native human heregulin- β 1 (SEQ ID NO: 93) numbered from the N-terminus and
- said heregulin variant comprises a portion that is at least 70% identical to the portion from about residue 175 to about residue 230 of native human heregulin- β 1 (SEQ ID NO: 93),
- said heregulin variant having a greater specificity for the ErbB-4 receptor, relative to the ErbB-3 receptor, than a heregulin that differs from the heregulin variant only in that the heregulin comprises said amino acid residues corresponding to residue numbers 228 to 231 in place of said methionine.
41. (New) The nucleic acid molecule of claim 40, said heregulin variant additionally comprising the amino acid substitution H178L.
42. (New) The nucleic acid molecule of claim 40, wherein said heregulin is a human heregulin.
43. (New) The nucleic acid molecule of claim 42, wherein said human heregulin is heregulin- β 1.
44. (New) The nucleic acid molecule of claim 40, wherein said heregulin variant is a fragment.
45. (New) The nucleic acid molecule of claim 44, wherein said fragment comprises residues corresponding to a portion of human heregulin- β 1 extending from about residue 175 to about residue 245.

46. (New) A vector comprising the nucleic acid molecule of claim 40.
47. (New) A host cell comprising the vector of claim 46.
48. (New) A method of producing a variant of a heregulin, said method comprising:
- (a) culturing the host cell of claim 47 under conditions that allow expression of the heregulin variant; and
 - (b) recovering the heregulin variant from the culture.
49. (New) A method of producing a heregulin variant comprising modifying the heregulin variant of claim 40 to produce a modified heregulin variant, wherein the modified heregulin variant retains the ability to bind an ErbB receptor.
50. (New) The method of claim 49, wherein said modifying step comprises introducing a modification selected from the group consisting of an amino acid substitution, an insertion of at least one amino acid, a deletion of at least one amino acid, and a chemical modification.
51. (New) A composition comprising the heregulin variant of claim 40 and a pharmaceutically acceptable carrier.
52. (New) A method for binding an ErbB receptor comprising contacting a variant of a heregulin with a cell that expresses said ErbB receptor, said variant having an amino acid sequence not found in nature and the ability to bind an ErbB receptor, wherein
- said variant comprises a methionine residue in place of amino acid residues corresponding to residue numbers 228 to 231 of native human heregulin- β 1 (SEQ ID NO: 93) numbered from the N-terminus and
 - said heregulin variant comprises a portion that is at least 70% identical to the portion from about residue 175 to about residue 230 of native human heregulin- β 1 (SEQ ID NO: 93),
 - said heregulin variant having a greater specificity for the ErbB-4 receptor, relative to the ErbB-3 receptor, than a heregulin that differs from the heregulin variant only in that the

heregulin comprises said amino acid residues corresponding to residue numbers 228 to 231 in place of said methionine.

53. (New) The method of claim 52, wherein said cell is in cell culture.

54. (New) The method of claim 52, wherein said cell is present in a mammal.

55. (New) The method of claim 54, wherein said mammal is a human.

56. (New) The method of claim 52, wherein said contacting enhances survival, proliferation, or differentiation of said cell.

57. (New) The method of claim 56, wherein said cell is selected from a glial cell, a Schwann cell, and muscle cell.

58. (New) The method of claim 52, wherein said heregulin is a human heregulin.

59. (New) The method of claim 58, wherein said human heregulin is heregulin- β 1.

60. (New) The method of claim 52, wherein said heregulin variant is a fragment.

61. (New) The method of claim 60, wherein said fragment comprises residues corresponding to a portion of human heregulin- β 1 extending from about residue 175 to about residue 245.

62. (New) The method of claim 52, wherein said heregulin variant is purified.

63. (New) A method of determining whether a sample contains an ErbB receptor that binds a heregulin comprising:

(a) contacting a variant of a heregulin with said sample; and

(b) determining whether said heregulin variant specifically binds a component of said sample as an indication of the presence of an ErbB receptor; said variant having an amino acid sequence not found in nature and the ability to bind an ErbB receptor, wherein said variant comprises a methionine residue in place of amino acid residues corresponding to residue numbers 228 to 231 of native human heregulin- β 1 (SEQ ID NO: 93) numbered from the N-terminus and said heregulin variant comprises a portion that is at least 70% identical to the portion from about residue 175 to about residue 230 of native human heregulin- β 1 (SEQ ID NO: 93), said heregulin variant having a greater specificity for the ErbB-4 receptor, relative to the ErbB-3 receptor, than a heregulin that differs from the heregulin variant only in that the heregulin comprises said amino acid residues corresponding to residue numbers 228 to 231 in place of said methionine.

64. (New) The method of claim 63, wherein said heregulin is a human heregulin.
65. (New) The method of claim 64, wherein said human heregulin is heregulin- β 1.
66. (New) The method of claim 63, wherein said heregulin variant is a fragment.
67. (New) The method of claim 66, wherein said fragment comprises residues corresponding to a portion of human heregulin- β 1 extending from about residue 175 to about residue 245.
68. (New) The method of claim 63, wherein said heregulin variant is purified.